## REMARKS

The above amendments to the above-captioned application along with the following remarks are being submitted as a full and complete response to the Official Action dated January 22, 2001, the period for response to which will expire on June 22, 2000.

In view of the above amendments and the following remarks, the Examiner is respectfully requested to give due reconsideration to this application, to indicate the allowability of the claims, and to pass this case to issue.

Claims 1-8, 11 and 19 are under consideration in this application. Claims 1, 7, 8, 11 and 19 are being amended, as set forth above and in the attached marked-up presentation of the claim amendments, in order to more particularly define and distinctly claim applicants' invention. New claims 20-21 are being added to recite other embodiments described in the specification. Applicants hereby submit that no new matter is being introduced into the application through the submission of this response.

### 35 U.S.C. §112 Rejection

Claims 1-8, 11 and 19 were rejected under the second paragraph of 35 U.S.C. § 112 because the Examiner does not understand how the 'mutually different' discrimination proceeds in the levels of DNAs selected from a database, the relevant partial sequences, primers, and hybridized DNAs. Also he believes the specification lacks sufficient support for mutually different DNAs selected from a database.

As indicated, claims 1, 7, 8, 11 and 19 have been amended so that the rejection should be obviated. Accordingly, the withdrawal of the outstanding indefiniteness rejection under 35 U.S.C. §112 is in order, and is therefore respectfully solicited.

### Prior Art Rejection

Claims 1-8, 11 and 19 were rejected under 35 U.S.C. §102 as being anticipated by an article written by Lowe et al. (hereinafter "Lowe"). The rejection has been carefully considered, but is most respectfully traversed.

The present invention is characterized in extracting a plurality of different genomic DNA nucleotide sequences (line 10, page 6) from human genomes (line 15, page 5); extracting a plurality of partial sequences from the different genomic DNA sequences which (1) meet extraction conditions (such as a predetermined base length, GC content or Tm), and (2) are extracted from different exons (associated with certain genetic functions or diseases; lines 18-19, page 5), while the genetic functions are still collated with the partial sequences; taking a plurality pairs of primers from the partial sequences; and synthesizing the primers, while the genetic functions are still collated with each of the primers. The base length is one of the extraction conditions executed independently from the conditions of GC content and Tm (Fig.5; p. 20).

Since a plurality of genomic DNA nucleotide sequences are extracted into a plurality of partial sequences, which are extracted from different exons, and then a plurality of primers are thereby determined, the present invention eliminates the possibility of repeating the extracting of the same exon twice such that the desired analysis of the primers and the relevant biological functions becomes more efficient (pages 2-6). As a result, the throughputs of the amplification and analysis are significantly improved by reducing redundant processing on the same primers. The present invention applies methods, such as computerized homology exclusion (Fig. 4) to reduce cross hybridization as much as possible. The partial sequences are not cross-hybridized so as to keep the associated genetic functions separated. As such, the genetic function(s) of a specific gene is provided as a result of predicted exons and homology exclusion between cDNA and known genes. Via the present invention, it becomes possible to design a plurality of potential primers without having to be limited to only one target DNA (Fig. 8; page 4, lines 21 to page 5).

In Embodiment 2 of the present invention, five conditions (page 35, lines 3-7) are used for screening the exons on genomic DNAs, positioning exons in genomic DNAs, and collating the exons with genetic functions via some off-the-shelf databases known to one skilled in the art. For example, GENSCAN, GRILL, or RE (page 18, line 9) may be used as an exon predicting program 304, ACTION may be used for ensuring the sequence of interest is in the expressed sequence tag (EST) database and can be expressed, and SWIS-PROT is used as a protein database. The genetic functions collated with the exons are further associated with the primers by tracking ID codes (line 5, page 29). In the case of cDNAs, exon prediction is not necessary since cDNAs are ligated from exons (Fig. 3; lines 24-27, page 17). The whole method of the present invention, especially the collating step, is performed "automatically" contrary to the prior

art that taught that two or more genetic functions can be "manually" collated with their corresponding pairs of primers.

Applicants respectfully contend that Lowe fails to teach or suggest extracting from a plurality of different genomic DNA sequences a plurality of partial sequences which are extracted from different exons (associated with certain genetic functions or diseases), and then synthesizing a plurality pairs of primers taken from the partial sequences while the genetic functions remain collated with the primers. In contrast, Lowe only requires a difference at the primer level (p. 2762, left col., line 3) but not at the levels of genomic DNAs or partial sequences. Further more, the primer selection criteria in Lowe includes predetermined base length, GC content and Tm but not being extracted from different exons.

Secondly, Lowe fails to teach or suggest processing a large plurality of different genomic DNAs (lines 4-14, page 27) to obtain a plurality sets of primers while automatically tracking the genetic functions collated with each of the partial sequences via off-the-shelf databases and with each of the primers via tracking ID codes. Lowe merely processes one gene or mRNA each time to obtain one set of primers. At most, any relevant genetic functions are maintained/collated manually for each pair of primer in Lowe. In particular, Lowe describes a method comprising searching 5' and 3' end regions of nucleotide sequences with a computer algorithm (page 1758, column 2, 1st paragraph), checking cross homology (page 1758, column 2, 3rd paragraph), and selecting a set of primers (page 1758, column 2, 4th paragraph). It is specified in this 4th paragraph that "a final primer set is then selected", which indicates only one primer set is obtained via the computer algorithm each time. The present invention, on the other hand, is intended to process a large plurality of different DNAs to obtain a plurality of primers, wherein the automated collating capability of the system allows a large scale analysis of primers that would otherwise be impossible to conduct manually while eliminating redundancies in the analysis.
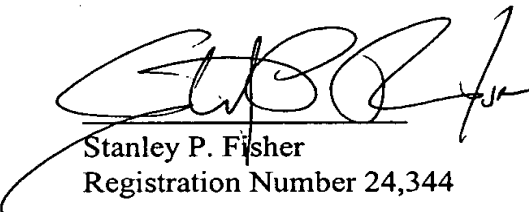
Since Lowe fails to teach or suggest what recited in claim 1, as discussed above, it is respectfully submitted that Lowe does not teach or suggest each and every element of the applicants' invention as now set forth in independent claims 1, 7-8, 11 and 19.

Accordingly, the withdrawal of the outstanding rejections under 35 U.S.C. §102 is in order, and is respectfully solicited.

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In view of all the above, clear and distinct differences as discussed exist between the present invention as now claimed and the prior art references upon which the rejections in the Office Action rely, Applicants respectfully contend that the prior art references cannot anticipate the present invention or render the present invention obvious. Rather, the present invention as a whole is distinguishable, and thereby allowable over the prior art.

Favorable reconsideration of this application as amended is respectfully solicited. Should there be any outstanding issues requiring discussion that would further the prosecution and allowance of the above-captioned application, the Examiner is invited to contact the Applicants' undersigned representative at the address and phone number indicated below.

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SPF/JCM/JT

1.    A primer design system, comprising:

means for selecting a [mutually different] plurality of [mutually] different DNA nucleotide sequences from a [first] database [having data on] including a plurality of [different] DNA nucleotide sequences of human genomes; and

a control unit for controlling the system, said control unit controlling:

means for extracting a plurality of partial sequences meeting [certain base length] extraction conditions from the plurality of different DNA nucleotide sequences, wherein said extraction conditions including a predetermined base length;

means for determining [the] positions of said plurality of partial sequences related to each one of said different DNA nucleotide sequences[, and conditions of each partial sequence's absence in DNA nucleotide sequences other than the DNA nucleotide sequence from which said each partial sequence is extracted], each of said plurality of different partial sequences being extracted from different exons;

means for selecting a plurality of [mutually] different partial sequences [meeting said conditions] from said plurality of partial sequences based on [the] results of said means for determining [means]; [and]

means for determining [taking at least one pair of primers for each of said plurality of mutually different DNA nucleotide sequences,] a plurality of pairs of primers for each of said plurality of [mutual] different [DNA nucleotide] partial sequences [from the results of said selecting capable of specifically amplifying said pair of primers to a plurality of hybridized DNA nucleotide sequences,]; and

[wherein] means for automatically collating said plurality of pairs of primers [are automatically collated] with genetic functions related to said different DNA nucleotide sequences respectively [from which they are extracted].

7.    A storage medium having recorded thereon a program executable at a control unit in a computer [having said control unit and] with memory [with] recording data on a plurality

of [mutually] different DNA nucleotide sequences <u>of human genomes</u>, said program comprising instruction<u>s</u>

for reading data on a plurality of [mutually] different DNA nucleotide sequences in said memory,

for extracting a plurality of partial sequences <u>meeting extraction conditions</u> [having a prescribed base length] from said plurality of <u>different</u> DNA nucleotide sequences [based on] and the data on said plurality of <u>different</u> DNA nucleotide sequences<u>, wherein said extraction conditions including a predetermined base length</u>,

for determining [the] positions of said plurality of partial sequences related to each one of said <u>different</u> DNA nucleotide sequences [and conditions of their absence in DNA nucleotide sequences other than said DNA nucleotide sequences]<u>, each of said plurality of different partial sequences being extracted from different exons</u>,

for selecting a plurality of [mutually] different partial sequences <u>from results of the determining step</u> [meeting said conditions], and

for <u>determining</u> [taking at least one pair of nucleotide sequences of primers for each of said plurality of mutually different DNA nucleotide sequences,] a plurality pairs of primers for <u>each of</u> said plurality of [mutual] different [DNA nucleotide] <u>partial</u> sequences [from the results of said selecting means capable of specifically amplifying said pair of primers to a plurality of hybridized DNA nucleotide sequences], <u>and</u>

[wherein] <u>for automatically collating</u> said plurality of pairs of primers [are automatically collated] with genetic functions related to said <u>different</u> DNA nucleotide sequences respectively [from which they are extracted].

8.    A method for designing primers, comprising the steps of:

<u>(a)</u> taking data on a plurality of [mutually] different DNA nucleotide sequences from a database including a plurality of different DNA nucleotide <u>sequences of human genomes;</u>

<u>(b)</u> extracting a plurality of partial sequences <u>meeting extraction conditions</u>[having a certain base length]  from <u>each of</u> said plurality of <u>different</u> DNA nucleotide sequences based on said [nucleotide sequence] data [obtained above]<u>, wherein said extraction conditions including a predetermined base length;</u>

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(c) determining [the] positions of said plurality of partial sequences related to each one of said plurality of different DNA nucleotide sequences[, and conditions of their absence in DNA nucleotide sequences other than said DNA nucleotide sequences];

(d) selecting a plurality of [mutually] different partial sequences [meeting said conditions] from said plurality of partial sequences, each of said plurality of different partial sequences being extracted from different exons [based on said determining results];

(e) after the step (d), determining [taking at least one pair of nucleotide sequences of primers for each of said plurality of mutually different DNA nucleotide sequences,] a plurality pairs of primers for each of said plurality of [mutual] different [DNA nucleotide] partial sequences [from the results of said selecting means capable of specifically amplifying said pair of primers to a plurality of hybridized DNA nucleotide sequences], and

(f) automatically collating said plurality of pairs of primers with genetic functions related to said different DNA nucleotide sequences respectively [from which they are extracted].

11. A method for designing primers, comprising the steps of

(a) taking data on a plurality of [mutually] different DNA nucleotide sequences from a database including a plurality of [different] DNA nucleotide sequences of human genomes;

(b) extracting a plurality of partial sequences meeting extraction conditions [having a certain base length] from each of said plurality of different DNA nucleotide sequences based on said [nucleotide sequence] data [obtained above], wherein said extraction conditions including a predetermined base length;

(c) determining certain conditions related to [the] positions of said plurality of partial sequences related to each one of said plurality of different DNA nucleotide sequences[, and conditions of their absence in DNA nucleotide sequences other than said DNA nucleotide sequences];

(d) selecting a plurality of [mutually] different partial sequences [meeting said conditions] from said plurality of partial sequences], each of said plurality of different

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partial sequences being extracted from different exons [based on said determining results];

(e) after the step (d), determining [taking at least one pair of primers for each of said plurality of mutually different DNA nucleotide sequences,] a plurality pairs of primers for each of said plurality of [mutual] different [DNA nucleotide] partial sequences [from the results of said selecting means capable of specifically amplifying said pair of primers to a plurality of hybridized DNA nucleotide sequences]; and

(f) analyzing a sample DNA using as an indicator for the type of primer affording PCR amplified fragments among said plurality of primers[, comprising] with a storage medium [and plurality of primers, the data for which have been recorded on said storage medium],

wherein said storage medium [comprising] comprises recorded data on said plurality pairs of primers [capable of specifically amplifying to mutually different DNAs], genetic data on DNA fragments amplified by PCR using said plurality pairs of primers, and [collating data between] said plurality of pairs of primers [and] automatically collated with genetic functions related to said different DNA nucleotide sequences [from which they are extracted].

19.     A primer design system, comprising:

means for selecting a [mutually different] plurality of [mutually] different DNA nucleotide sequences based on at least one predetermined genetic function of interest from a [first] database having data on a plurality of [different] DNA nucleotide sequences of human genomes; and

a control unit for controlling the system, said control unit controlling:

means for extracting a plurality of partial sequences meeting certain base length extraction conditions from the plurality of different DNA nucleotide sequences [and the data of said genetic functions of interest];

means for determining [the] positions of said plurality of partial sequences related to each one of said plurality of different DNA nucleotide sequences[, and conditions of each partial sequence's absence in DNA nucleotide sequences other than the DNA nucleotide sequence from which said each partial sequence is extracted];

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means for selecting a plurality of [mutually] different partial sequences [meeting said conditions] from said plurality of partial sequences, each of said plurality of different partial sequences being extracted from different exons [based on results of said determining means]; and

means for determining [taking at least one pair of primers for each of said plurality of mutually different DNA nucleotide sequences,] a plurality pairs of primers for each of said plurality of [mutual] different [DNA nucleotide] partial sequences [from the results of said selecting means capable of specifically amplifying said pair of primers to a plurality of hybridized DNA nucleotide sequences,]; and

[wherein] means for automatically collating said plurality of pairs of primers [are automatically collated] with said genetic functions of interest related to said different DNA nucleotide sequences respectively [from which they are extracted].